

IN THE CLAIMS

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Claim 1 (Cancelled)

2 (Original and withdrawn). A nucleotide sequence represented by the 272nd to 958th bases of SEQ ID NO:1; a nucleotide sequence encoding the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:2; or a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:2.

Claims 3-19 (Cancelled)

D 20 (Previously amended and withdrawn). A vector comprising the nucleotide sequence according to claim 43.

21 (Previously amended and withdrawn). Transformed cells having the nucleotide sequence according to claim 43 in an expressible state.

22 (Previously amended and withdrawn). A process for producing a protein which comprises culturing cells transformed with the nucleotide sequence (aa), (bb), (cc), (gg), (hh), (ii), (jj), (kk), (ll), (yy) or (zz) of claim 43, and collecting hBSSP6 produced.

Claims 23 and 24 (Cancelled)

25(Previously amended and withdrawn). The process according to claim 22, wherein the cells are *E. coli* cells, animal cells or insect cells.

26(Original and withdrawn). A non-human transgenic animal whose expression level of BSSP6 gene has been altered.

27(Original and withdrawn). The non-human transgenic animal according to claim 26, wherein BSSP6 gene is cDNA, genomic DNA or synthetic DNA encoding BSSP6.

28(Original and withdrawn). The non-human transgenic animal according to claim 26, wherein the expression level has been altered by mutating a gene expression regulatory site.

29(Original and withdrawn). A knockout mouse whose BSSP6 gene function is deficient.

30(Previously amended). An antibody against the protein according to claim 42 or a fragment thereof.

31(Original). The antibody according to claim 30 which is a polyclonal antibody, a monoclonal antibody or a peptide antibody.

32(Previously amended and withdrawn). A process for producing a monoclonal antibody against the protein according to claim 42 or a fragment thereof which comprises administering the protein according to claim 42 or a fragment thereof to a warm-blooded animal other than a human being, selecting the animal whose antibody titer is recognized, collecting its spleen or

lymph node, fusing the antibody producing cells contained therein with myeloma cells to prepare a monoclonal antibody producing hybridoma.

33 (Previously amended and withdrawn). A method for determining the protein according to claim 42 or a fragment thereof in a specimen which is based on immunological binding of an antibody against the protein or a fragment thereof to the protein or a fragment thereof.

34 (Previously amended and withdrawn). A method for determining BSSP6 or a fragment thereof in a specimen which comprises reacting a monoclonal antibody or a polyclonal antibody against the protein (a), (b), (e), (f), (g), (h), (m), (n), (o) or (p) of claim 42 or a modified derivative thereof or a fragment thereof and a labeled antibody with BSSP6 or a fragment thereof in the specimen to detect a sandwich complex produced.

D' 35 (Previously amended and withdrawn). A method for determining BSSP6 or a fragment thereof in a specimen which comprises reacting a monoclonal antibody or a polyclonal antibody against the protein (a), (b), (e), (f), (g), (h), (m), (n), (o) or (p) of claim 42 or a modified derivative thereof or a fragment thereof with labeled BSSP6 and BSSP6 or a fragment thereof in the specimen competitively to detect an amount of BSSP6 or a fragment thereof in the specimen based on an amount of the labeled BSSP6 reacted with the antibody.

36 (Previously amended and withdrawn). The method according to claim 33, wherein the specimen is a body fluid.

37 (Currently amended). A method for detecting a disease which comprises measuring concentration, in blood or urine, of a protein as a diagnostic marker selected from the group consisting of: A diagnostic marker for diseases in tissues comprising the protein according to claim 42, or a fragment thereof.

(a) a protein having the amino acid sequence composed of 229 amino acid represented by residues 54 to 282 of SEQ ID NO:2 and having the serine protease activity;

(b) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 272 to 958 of SEQ ID NO:1 under stringent conditions, and having the same serine protease activity as that of the protein (a);

(c) a protein having the amino acid sequence composed of 229 amino acids represented by residues 48 to 276 of SEQ ID NO:4 and having the serine protease activity;

(d) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 244 to 930 of SEQ ID NO:3 under stringent conditions, and having the same serine protease activity as that of the protein (c);

(e) a protein having the amino acid sequence composed of 249 amino acids represented by residues 28 to 276 of SEQ ID NO:4 and, a mature form of which has the same serine protease activity as that of the protein (c);

(f) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 184 to 930 of SEQ ID NO:3 under stringent conditions and, a mature form of which has the same serine protease activity as that of the protein (c);

(g) a protein having the amino acid sequence composed of 276 amino acids represented by residues 1 to 276 of SEQ ID NO:4 and, a mature form of which has the same serine protease activity as that of the protein (c);

(h) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 103 to 930 of SEQ ID NO:3 under stringent condition, and a mature form of which has the same serine protease activity as that of the protein (c);

(i) a protein having the amino acid sequence composed of 254 amino acids represented by residues 22 to 275 of SEQ ID NO:6 and having the serine protease activity;

(j) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 114 to 875 of SEQ ID NO:5 under stringent conditions, and having the same serine protease activity as that of the protein (i);

(k) a protein having the amino acid sequence composed of 275 amino acids represented by residues 1 to 275 of SEQ ID NO:6 and, a mature form which has the same serine protease activity as that of the protein (i);

(l) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 51 to 875 of SEQ ID NO:5 under stringent conditions, and a mature form of which has the same serine protease activity as that of the protein (i); and

(m) a modified derivative or fragment of those proteins (a) to (l).

38(Currently amended). The method ~~marker~~ according to claim 37, wherein the disease is to be used for diagnosis of Alzheimer's disease or epilepsy in the brain.

39(Currently amended). The method ~~marker~~ according to claim 37, to be used for diagnosis of is cancer or inflammation of brain, medulla, prostate, placenta, heart, testicle or lung.

D 40(Currently amended). The ~~marker~~ method according to claim 37, to be used for diagnosis of wherein the disease is sterility in semen or sperms.

41(Previously amended). The marker according to claim 37 to be used for diagnosis of prostatic hypertrophy in prostate.

42(Currently amended). A protein selected from the group consisting of:

(a) ~~a protein having the amino acid sequence composed of 229 amino acids represented by the 1st to 229th amino acids~~ consisting of residues 54 to 282 of SEQ ID NO:2 and having the serine protease activity;

(b) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 272 having a nucleotide sequence represented by nucleotides 272 to 958 of SEQ ID NO:1 under stringent conditions, and having the same serine protease activity as that of the protein (a); ~~having an amino acid sequence derived from the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:2 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:2;~~

(c) a protein having the amino acid sequence composed of 229 amino acids represented by residues 48 to 276 ~~the 1st to 229th amino acids~~ of SEQ ID NO:4 and having the serine protease activity;

D (d) a protein ~~having~~ encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 244 to 930 ~~an amino acid sequence derived from the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:4~~ under stringent conditions, and having the same serine protease activity as that of the protein (c); ~~by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:4;~~

(e) a protein having the amino acid sequence composed of 282 249 amino acids represented by residues 28 to 276 ~~the~~

53rd to 229th amino acids of SEQ ID NO:24 and, a mature form of which has the same serine protease activity as that of the protein (c);

(f) a protein having encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 184 to 930 an amino acid sequence derived from the amino acid sequence represented by the 53rd to 229th amino acids of SEQ ID NO:23 under stringent conditions and, a mature form of which has the same serine protease activity as that of the protein (c); by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 53rd to 229th amino acids of SEQ ID NO:27;

D (g) a protein having the amino acid sequence composed of 250 276 amino acids represented by residues 1 to 276 the 21st to 229th amino acids of SEQ ID NO:24 and, a mature form of which has the same serine protease activity as that of the protein (c);

(h) a protein having encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 103 to 930 an amino acid sequence derived from the amino acid sequence represented by the 21st to 229th amino acids of SEQ ID NO:23 under stringent condition, and a mature form of which has the same serine protease activity as that of the protein (c); by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the



~~amino acid sequence represented by the 21st to 229th amino acids of SEQ ID NO:2;~~

(i) a protein having the amino acid sequence composed of ~~249~~ 254 amino acids represented by residues 22 to 275 ~~the 20th to 229th amino acids~~ of SEQ ID NO:46 and having the serine protease activity;

(j) a protein ~~having~~ encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 114 to 875 ~~an amino acid sequence derived from the amino acid sequence represented by the 20th to 229th amino acids of SEQ ID NO:45~~ under stringent conditions, and having the same serine protease activity as that of the protein (i) ~~by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 20th to 229th amino acids of SEQ ID NO:4;~~

D (k) a protein having the amino acid sequence composed of ~~276~~ 275 amino acids represented by residues 1 to 275 ~~the 47th to 229th amino acids of SEQ ID NO:46~~ and, a mature form which has the same serine protease activity as that of the protein (i);

(l) a protein ~~having~~ encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 51 to 875 ~~an amino acid sequence derived from the amino acid sequence represented by the 47th to 229th amino acids of SEQ ID NO:45~~ under stringent conditions, and a mature form of which has the same serine protease activity as that of the protein (i); and by deletion, substitution or addition of one to several amino acids

~~and having the same property as that of the protein having the amino acid sequence represented by the 47th to 229th amino acids of SEQ ID NO:4;~~

~~(m) a modified derivative or fragment of those proteins (a) to (l). protein having the amino acid sequence composed of 254 amino acids represented by the 1st to 254th amino acids of SEQ ID NO:6;~~

~~(n) a protein having an amino acid sequence derived from the amino acid sequence represented by the 1st to 254th amino acids of SEQ ID NO:6 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 1st to 254th amino acids of SEQ ID NO:6;~~

~~(o) a protein having the amino acid sequence composed of 275 amino acids represented by the 21st to 254th amino acids of SEQ ID NO:6; and~~

~~(p) a protein having an amino acid sequence derived from the amino acid sequence represented by the 21st to 254th amino acids of SEQ ID NO:6 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 21st to 254th amino acids of SEQ ID NO:6; and~~

~~(q) a modified derivative or fragment of these proteins (a) to (p).~~

43 (Previously added and withdrawn). A nucleotide sequence selected from the group consisting of:

(aa) a nucleotide sequence of nucleotides 272 to 958 of SEQ ID NO:1;

(bb) a nucleotide sequence encoding the amino acid sequence of residues 1 to 229 of SEQ ID NO:2;

(cc) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (aa) or (bb) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues 1 to 229 of SEQ ID NO:2;

(dd) a nucleotide sequence of nucleotides 244 to 930 of SEQ ID NO:3;

(ee) a nucleotide sequence encoding the amino acid sequence of residues 1 to 229 of SEQ ID NO:4;

D (ff) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (dd) or (ee) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues 1 to 229 of SEQ ID NO:4;

(gg) a nucleotide sequence of nucleotides 113 to 958 of SEQ ID NO:1;

(hh) a nucleotide sequence encoding the amino acid sequence of residues -53 to 229 of SEQ ID NO:2;

(ii) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (gg) or (hh) under stringent conditions and encoding a protein having the same property as that of the

protein having the amino acid sequence of residues -53 to 229 amino acids of SEQ ID NO:2;

(jj) a nucleotide sequence of nucleotides 209 to 958 of SEQ ID NO:1;

(kk) a nucleotide sequence encoding the amino acid sequence of residues -21 to 229 of SEQ ID NO:2;

(ll) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (jj) or (kk) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -21 to 229 of SEQ ID NO:2;

(mm) a nucleotide sequence of nucleotides 184 to 930 of SEQ ID NO:3;

(nn) a nucleotide sequence encoding the amino acid sequence of residues -20 to 229 of SEQ ID NO:4;

(oo) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (mm) or (nn) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -20 to 229 of SEQ ID NO:4;

(pp) a nucleotide sequence of nucleotides 103 to 930 of SEQ ID NO:3;

(qq) a nucleotide sequence encoding the amino acid sequence of residues -47 to 229 of SEQ ID NO:4;

(rr) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above

nucleotide sequence (pp) or (qq) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -47 to 229 of SEQ ID NO:4.

(ss) a nucleotide sequence of nucleotides 114 to 875 of SEQ ID NO:5;

(tt) a nucleotide sequence encoding the amino acid sequence of residues 1 to 254 of SEQ ID NO:6;

(uu) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (ss) or (tt) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues 1 to 254 of SEQ ID NO:6;

(vv) a nucleotide sequence of nucleotides 51 to 875 of SEQ ID NO:5;

D (ww) a nucleotide sequence encoding the amino acid sequence of residues -21 to 254 of SEQ ID NO:6;

(xx) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (vv) or (ww) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -21 to 254 of SEQ ID NO:6;

(yy) a nucleotide sequence of SEQ ID NO:1;

(zz) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (yy) under stringent conditions and encoding

a protein having the same property as that of the protein encoded by the nucleotide sequence of SEQ ID NO:1;

(aaa) a nucleotide sequence of SEQ ID NO:3;

(bbb) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (aaa) under stringent conditions and encoding a protein having the same property as that of the protein encoded by the nucleotide sequence of SEQ ID NO:3;

(ccc) a nucleotide sequence of SEQ ID NO:5;

(ddd) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (ccc) under stringent conditions and encoding a protein having the same property as that of the protein encoded by the nucleotide sequence of SEQ ID NO:5; and

(eee) a fragment of these nucleotide sequences (aa) to (ddd).

D 44(Previously added and withdrawn). A process for producing a protein which comprises culturing cells transformed with the nucleotide sequence (dd), (ee), (ff), (mm), (nn), (oo), (pp), (qq), (rr), (aaa) or (bbb) of claim 43, and collecting mBSSP6 produced.

45(Previously added and withdrawn). The process according to claim 44, wherein the cells are *E. coli* cells, animal cells or insect cells.

46(Previously added and withdrawn). A process for producing a protein which comprises culturing cells transformed

with the nucleotide sequence (ss), (tt), (uu), (vv), (ww), (xx), (ccc) or (ddd) of claim 43 and collecting mutant hBSSP6 produced.

47(Previously added and withdrawn). The process according to claim 46, wherein the cells are *E. coli* cells, animal cells or insect cells.

48(Previously added and withdrawn). The method according to claim 34, wherein the specimen is a body fluid.

49(Previously added and withdrawn). The method according to claim 35, wherein the specimen is a body fluid.

D 50(Previously added and withdrawn). A method for screening for an inhibitor of serine protease comprising comparing the enzyme activity of the protein according to claim 42 upon bringing the protein into contact with a candidate compound with the enzyme activity of the protein without contact with the candidate compound.

51(Previously added). A pharmaceutical composition comprising the protein according to claim 42.

52(Previously added and withdrawn). A method for detecting a diagnostic marker for diseases in tissues comprising the protein according to claim 42 which comprises using the antibody against the protein according to claim 42.

53(Previously added and withdrawn). The method according to claim 52, wherein the marker is used for diagnosis of a cancer.

54(New). An immunohistochemical method for detecting a protein as a diagnostic marker for a certain disease selected from the group consisting of:

(a) a protein having the amino acid sequence composed of 229 amino acids represented by residues 54 to 282 of SEQ ID NO:2 and having the serine protease activity;

(b) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 272 to 958 of SEQ ID NO:1 under stringent conditions, and having the same serine protease activity as that of the protein (a)

(c) a protein having the amino acid sequence composed of 229 amino acids represented by residues 48 to 276 of SEQ ID NO:4 and having the serine protease activity;

D<sup>1</sup> (d) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 244 to 930 of SEQ ID NO:3 under stringent conditions, and having the same serine protease activity as that of the protein (c),

(e) a protein having the amino acid sequence composed of 249 amino acids represented by residues 28 to 276 of SEQ ID NO:4 and, a mature form of which has the same serine protease activity as that of the protein (c)

(f) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 184 5 to 930 of SEQ ID NO: 3 under stringent conditions and, a mature



form of which has the same serine protease activity as that of the protein (c)

(g) a protein having the amino acid sequence composed of 276 amino acids represented by residues 1 to 276 of SEQ ID No:4 and, a mature form of which has the same serine protease activity as that of the protein (c)

(h) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 103 to 930 of SEQ ID NO:3 under stringent condition, and a mature form of which has the same serine protease activity as that of the protein (c);

(i) a protein having the amino acid sequence composed of 254 amino acids represented by residues 22 to 275 of SEQ ID NO:6 and having the serine protease activity;

D (j) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 114 to 875 of SEQ ID NO:5 under stringent conditions, and having the same serine protease activity as that of the protein (i);

(k) a protein having the amino acid sequence composed of 275 amino acids represented by residues 1 to 275 of SEQ ID No:6 and, a mature form which has the same serine protease activity as that of the protein (i);

(l) a protein encoded by a nucleotide which is hybridizable to a nucleotide complementary to a nucleotide having a nucleotide sequence represented by nucleotides 51

to 875 of SEQ ID NO:5 under stringent conditions, and a mature form of which has the same serine protease activity as that of the protein (i); and

(m) a modified derivative or fragment of those proteins (a) to (l),  
comprising:

a) taking a tissue specimen from a subject suspected of suffering from the disease;

b) reacting the antibody against the protein with the diagnostic marker;

c) detecting the diagnostic maker in the tissue specimen by the reaction of b); and

d) conducting diagnosis of the disease by evaluating immunoreactivity between the antibody and said tissue specimen.

D 55(New). The method according to claim 54, wherein the disease is Alzheimer's disease or epilepsy in the brain.

56(New). The method according to claim 54, wherein the disease is cancer or inflammation of brain, medulla, prostate, placenta, heart, testicle or lung.

57(New). The method according to claim 54, wherein the disease is sterility in semen or sperm.

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